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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/395,677	09/13/99	BERGER	P-4579

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EXAMINER

FORMAN, B

ART UNIT	PAPER NUMBER
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1655

DATE MAILED: 09/22/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/395,677

Applicant(s)

BERGER ET AL.

Examiner

BJ Forman

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

- 1) ☒ Responsive to communication(s) filed on 21 August 2000.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-32 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-32 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some * c) ☐ None of the CERTIFIED copies of the priority documents have been:
- ☐ received.
 - ☐ received in Application No. (Series Code / Serial Number) _____.
 - ☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

- 15) ☒ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5.
- 18) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other: _____

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DETAILED ACTION

1. This action is in response to papers filed 21 August 2000 in Paper No. 8 in which claims 1 and 13 were amended. All of the amendments have been thoroughly reviewed and entered. The previous rejections under 35 U.S.C. 112, second paragraph are withdrawn in view of the amendments. The previous rejections under 35 U.S.C. 102(e) and 35 U.S.C. 103(a) are withdrawn in view of the amendments. All of the arguments have been thoroughly reviewed. All arguments are deemed moot in view of the amendments and new grounds for rejection.

New grounds for rejection are discussed.

Currently claims 1-32 are under prosecution.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

First paragraph of 35 U.S.C. 112: New Matter

3. Claims 1-32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims as amended are drawn to a method for stabilizing the structure and nucleic acids of at least one cell in a sample comprising adding to a vessel containing the sample a substance effective for precipitating or denaturing proteins and effective for aiding in the infusion of said composition into said at least one cell wherein the concentration of said substance is greater than 30% of the composition (Claims 1-12) and wherein the composition comprises a first substance effective for precipitating or denaturing

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proteins and a second substance effective for aiding in the infusion of said first substance into said at least one cell (Claims 13-32). However, the specification teaches the concentration of the substance is 20%, 40%, 50%, 80% or 100%. And the specification teaches the concentration of said first and second substance is always 100% (page 4, lines 19-24, Examples 4 through 13). The specification does not teach the concentration of the substance is greater than 30% as claimed and the specification does not teach the combined concentration is greater than 30%. Therefore the claims, as amended, introduce new matter not disclosed in the specification as originally filed. It is suggested that the claims be amended to claim the invention as recited in the originally filed specification.

First paragraph of 35 U.S.C. 112: Written Description

4. Claims 1-32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims, as amended, are drawn to a method for stabilizing the structure and nucleic acids of at least one cell in a sample. The specification teaches the claimed method for stabilization of cells in a vaginal swab samples (page 7, lines 7-9 and 24-26). Additionally, the specification teaches specific cell types found in vaginal fluid i.e. *Trichomonas vaginalis*, *Gardnerella vaginalis* and *Candida albican* and the specification teaches the claimed methods stabilize the structure and nucleic acids in these cell types (pages 11-12, Examples 2 & 4-12). The specification suggests the method "could be used for other biological specimens" (page 4, lines 26-29). However, the specification does not teach the method stabilizes the structure and nucleic acids of other specimens in the very large genus of cells as claimed. The claimed cells encompasses eukaryotic cells which further encompasses plant and animal cells each of which further encompass numerous species and sub-species,

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prokaryotic cells which further encompasses bacteria which further encompasses numerous species not described in the specification. The specification fails to teach a representative number of the claimed species. The specification teaches various formulations of the claimed method composition and experimental conditions using the compositions (Examples 4-12) but the specification does not teach using the claimed method with a representative number of the claimed cell species. Therefore, the specification does not provide a written description of the claimed composition in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The courts have stated that the specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonable conclude the inventor had possession of the claimed invention see *In re Vas-Cath, Inc.* 935F2d. 1555, 1563, 19 USPQ2d 1111,1116. It is suggested that the claims be amended to claims the invention as described in the specification e.g. by inserting "in vaginal fluid" after "one cell" in line 2 of Claim 1 and Claim 13.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1-5, 7-17, 21 & 25-31 are rejected under 35 U.S.C. 102(b) as clearly anticipated by Dent et al (Development, 1989, 105: 61-74).

Regarding Claim 1, Dent et al. disclose a method for stabilizing the structure and nucleic acids of at least one cell in a sample comprising adding to a vessel containing the sample a composition comprising a substance capable of precipitating or denaturing proteins and capable of aiding in the infusion of said composition into said cell i.e. methanol, wherein

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the concentration of said substance is greater than 30%; contacting said cell in said sample with said composition; incubating said sample with said composition for an effective period of time and at an effective temperature and obtaining said at least one cell with stabilized structure and nucleic acids (page 62, right column, last paragraph).

Regarding Claim 2-3, Dent et al. disclose the method of Claim 1 wherein said substance is methanol (page 62, right column, last paragraph, line 7).

Regarding Claim 4, Dent et al. disclose the method of Claim 1 wherein said substance is DMSO (page 62, right column, last paragraph, line 7).

Regarding Claim 5, Dent et al. disclose the method of Claim 1 wherein said cell is a eukaryote (page 62, right column, last paragraph).

Regarding Claims 7-9, Dent et al. disclose the method of Claim 1 wherein all the cellular nucleic acids are stabilized i.e. DNA, RNA and ribosomal RNA (page 62, right column, last paragraph).

Regarding Claim 10, Dent et al. disclose the method of Claim 1 wherein the effective period of time is from about one to four days (page 62, right column, last paragraph, lines 7-10).

Regarding Claims 11-12, Dents et al. disclose the method of Claim 1 wherein the effective temperature is room temperature which is between 0°C and 40°C (page 62, right column, last paragraph, line 10).

Regarding Claim 13, Dent et al. disclose a method for stabilizing the structure and nucleic acids of at least one cell in a sample comprising; adding to a vessel containing the sample a composition comprising a first substance having an effective concentration for precipitating or denaturing proteins i.e. methanol and a second facilitator substance having an effective concentration for aiding in the infusion of said first substance into said cell i.e. DMSO, wherein the combined concentration of said first and second substances is greater than 30%; contacting said cell in said sample with said composition; incubating said sample with said

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composition for an effective period of time and at an effective temperature and obtaining said at least one cell with stabilized structure and nucleic acids (page 62, right column, last paragraph).

Regarding Claim 14, Dent et al. disclose the method of Claim 13 wherein said first substance is methanol (page 62, right column, last paragraph, line 7).

Regarding Claim 15, Dent et al. disclose the method of Claim 13 wherein said second substance is DMSO (page 62, right column, last paragraph, line 7).

Regarding Claim 16, Dent et al. disclose the method of Claim 13 wherein said first substance is comprised of one alcohol i.e. methanol (page 62, right column, last paragraph, line 7).

Regarding Claim 17, Dent et al. disclose the method of Claim 13 wherein the concentrations of said first and said second substances are in a ration of 4:1 (page 62, right column, last paragraph, line 7).

Regarding Claim 21, Dent et al. disclose the method of Claim 13 wherein said first substance is methanol and said second substance is DMSO (page 62, right column, last paragraph, lines 6-7).

Regarding Claims 25-27, Dent et al. disclose the method of Claim 13 wherein all the cellular nucleic acids are stabilized i.e. DNA, RNA and ribosomal RNA (page 62, right column, last paragraph).

Regarding Claim 28, Dent et al. disclose the method of Claim 13 wherein the effective period of time is from about one to four days (page 62, right column, last paragraph, lines 7-10).

Regarding Claims 29-30, Dent et al. disclose the method of Claim 13 wherein the effective temperature is room temperature which is between 0°C and 40°C (page 62, right column, last paragraph, line 10).

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Regarding Claim 31, Dent et al. disclose the method of Claim 13 wherein the cell is a eukaryote (page 62, right column, last paragraph, line 10).

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. Claims 6 & 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dent et al. (Development, 1989, 105: 61-74) as applied to Claims 1 & 13 above and further in view of Bresser et al. (U.S. Patent No. 5,521,061, filed 17 July 1992).

Regarding Claims 6 & 32, Dent et al. teach the methods of Claims 1 and 13 wherein said cell is a eukaryote (page 62, right column, last paragraph, lines 1-2) but they do not teach the cell is a microorganism. However, Bresser et al. teach a similar method for stabilizing the structure and nucleic acids of a cell wherein the cell may be simple or complex i.e. eukaryote, prokaryote or a microorganism (Column 6, lines 14-18). It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the method of Dent et al. with the teachings of Bresser et al. to obtain the claimed invention because the skilled practitioner in the art would have been motivated with a reasonable expectation of success to apply the method of Dent et al. to microorganisms based on the teaching of Bresser et al. and to prepare one composition for the stabilizing structure and nucleic acids in any cell type for the obvious benefit of convenience.

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9. Claims 18, 19 & 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dent et al. (Development, 1989, 105: 61-74) as applied to Claim 13 above and further in view of Bresser et al. (U.S. Patent No. 5,521,061, files 17 July 1992). Dent et al. disclose a composition comprising a first substance capable of precipitating i.e. an alcohol and a second substance to aid in the infusion of the first substance (page 62, right column, last paragraph, lines 6-7).

Regarding Claim 18, Dent et al. do not teach the composition wherein the first substance is comprised of a first alcohol and a second alcohol. However, Bresser et al. teach a similar composition wherein the first substance is comprised of a first alcohol i.e. dithiothreitol and a second alcohol i.e. polyethylene glycol (Column 9, lines 6-17).

Regarding Claim 19, Bresser et al. do not teach the composition wherein the ratio of the first and second substances are 2.5:2.5:5. However, Bresser et al. teach the composition wherein 2-20 percent of the composition is said first substance i.e. an alcohol and wherein 2-20 percent of the composition is said second substance i.e. dimethyl sulfoxide. It would have been known to one of ordinary skill in the art that the percentages taught by Bresser et al. include the 2.5:2.5:5 ratio e.g. 2%:2%:5% or 4%:4%:16% etc.

Regarding Claim 22, Bresser et al. teach the composition wherein said first substance is a precipitating agent i.e. alcohol and said second substance is dimethyl sulfoxide (Claim 54, lines 1-3). It was known to one of skill in the art at the time the claimed invention was made that ethanol and methanol are precipitating agents as taught by Bresser et al. (Column 7, line 40).

It would have been *prime facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the method of Dent et al. with the teaching of Bresser et al. to obtain the claimed invention because one of ordinary skill in the art would have been motivated with a reasonable expectation of success to modify the alcohol in the composition of Dent et al. with the specific teaching of Bresser et al. wherein the alcohol is selected from the group consisting of ethanol and methanol to use ethanol and methanol in the composition at

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the ratio of 2.5:2.5:5 based on cell type being assayed, available reagents and known precipitating properties.

10. Claims 20 & 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dent et al. (Development, 1989, 105: 61-74) as applied to Claim 13 & 16 above and further in view of Bresser et al. (U.S. Patent No. 5,521,061, filed 17 July 1992). Dent et al. disclose a composition comprising a first substance capable of precipitating i.e. an alcohol and a second substance to aid in the infusion of the first substance (page 62, right column, last paragraph, lines 6-7).

Regarding Claim 20, Dent et al. do not teach a 1:1 ratio of said first and second substance. However, Bresser et al. teach a similar composition wherein 2-20 percent of the composition is said first substance i.e. an alcohol and wherein 2-20 percent of the composition is said second substance i.e. dimethyl sulfoxide. It would have been known to one of ordinary skill in the art that the percentages taught by Bresser et al. include the 1:1 ratio.

Regarding Claim 24, Dent et al. teach the composition wherein said first substance is methanol and said second substance is dimethyl sulfoxide (page 62, right column, last paragraph, lines 6-7).

It would have been *prime facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the composition of Dent et al. with the teaching of Bresser et al. to obtain the claimed invention because the skilled practitioner would have been motivated with a reasonable expectation of success to modify the methanol to dimethyl sulfoxide ratio of Dent et al. based on the range of concentration percentages taught by Bresser et al. for the obvious benefit of optimizing experimental conditions to maximize experimental results. It is noted that *In re Aller*, 220 F.2d 454,456, 105 USPQ 233,235 states where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum by routine experimentation.

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11. Claim 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over Dent et al. (Development, 1989, 105: 61-74) as applied to Claims 13 & 17 above. Dent et al. disclose a composition comprising a first substance capable of precipitating proteins comprising an i.e. methanol (page 62, right column, last paragraph, lines 6-7) but they do not teach the alcohol is ethanol. However, it was known in the art at the time the claimed invention was made that methanol and ethanol were homologues having similar precipitating properties. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the method of Dent et al. with the known methanol homologous to obtain the claimed invention because the skilled practitioner in the art would have been motivated with a reasonable expectation of success to use methanol and/or ethanol in the composition Dent et al. based on their known similarities and based on available reagents.

Response to Arguments

12. Applicant argues that Bresser et al. do not teach, disclose or anticipate every element of the claims as amended, but in fact teach away from the claimed invention as amended. These arguments are mooted in view of the amendments and new grounds for rejection.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

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CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.


Conclusion


14. No claim is allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:45 TO 4:15.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-8742 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.


BJ Forman, Ph.D.
September 21, 2000


W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600
9/21/00